REMARKS

1. The Amendments and the Support Therefor

No claims have been canceled, six new claims (71-76) have been added, and claims 1, 14, 27, and 40 have been amended to leave claims 1-5, 7-18, 20-31, 33-44, 46-52, and 67-76 in the application. A form PTO-2038 authorizing a charge for any newly-submitted claims in excess of the amount previously paid for should accompany this Response, as per 37 CFR §1.16(b)-(d), with the fee due being calculated as follows:

FEE CALCULATION

For	Already Paid	No. Extra	Rate (SMALL ENTITY)	Fee (SMALL ENTITY)
Total Claims	58 - 52 =	6	x $9 =	$54
Independent Claims	6 - 4 =	2	x $42 =	$84
2-Mo. Extension				$205
			Total:	$343

No new matter has been added by the amendments or new claims, with the amendments merely further clarifying the previously-recited limitations (as discussed in Section 2 of this Response) and new claims 71-76 finding basis (for example) in claims 1, 7, and 9.

2. Sections 1-2 of the Office Action: Rejection of Claims 1-5, 8, 10-19, 21, 23-31, 34, 36-44, 47, 49-52, and 67-70 under 35 USC §103(a) in view of *Drobyshev et al* (Gene (1997) 188:45-52) and U.S. Patent 6,174,670 to *Wittwer*

The Examiner asserts that it would be *prima facie* obvious to one of skill in the art to employ the SYBR Green markers of *Wittwer* in the method of *Drobyshev*, and thereby obtain a method in accordance with the present claims. In particular, the Examiner asserts that the claimed "single DNA strand of a double stranded DNA of at least 40 base pairs containing the locus of a variation, bound to a solid surface" encompasses the gel immobilized 10-mer oligonucleotides of *Drobyshev*, alleging that:

(1) a polyacrylamide gel constitutes a "solid surface" as claimed (pages 8-9 of the Office Action);

(2) even if *Drobyshev*'s polyacrylamide gel is not a "solid surface", giving the "broadest reasonable interpretation" to the term "bound," *Drobyshev*'s oligonucleotide is *indirectly* bound to a solid surface (glass), which corresponds to the claimed arrangement (pages 9-10 of the Office Action); and

(3) by arguing that the 3D arrangement of *Drobyshev* is not equivalent to a single layer of oligonucleotides bound to a solid surface, the Applicant argues unclaimed limitations (page 10 of the Office Action).

Regarding point (3), the claims have been amended to recite that the strand is bound to the surface *within a monolayer*, thereby obviating this point of rejection.[1] Regarding points (1) and (2), kindly reconsider in view of the following.

2.a. The Cited References Do Not Disclose, or Objectively Suggest, Solid-Phase Nucleic Acid *Surface* Hybridization

The Applicant has maintained that in the field of the invention, which is nucleic acid hybridization, a polyacrylamide gel is not a "solid surface" as recited in the present claims. The Examiner has maintained otherwise, citing to U.S. Publication US2002/0109841, *Drobyshev*, and the ordinary meaning of "solid surface." Kindly reconsider in light of the following discussion.

2.a.i. U.S. Publication US2002/0109841, When Viewed in Context, Does Not Disclose or Suggest that a Polyacrylamide Gel is a Solid Surface

The Examiner has cited US02/0109841 as evidence that the term "solid surface" may encompass a polyacrylamide gel. However, with all respect, this assertion is flawed in two respects.

First, the reference is nonanalogous art as per MPEP 2141.01(a), and thus its contents and terminology do not speak to what one of ordinary skill *in the art of the present invention* would understand "surface" to encompass. US02/0109841 relates to analytical instrumentation for

[1] We submit that the "monolayer" limitation is unnecessary since a surface is, by definition, the two-dimensional outer boundary of a three-dimensional object. Therefore, those oligonucleotides bound to the 2D surface will necessarily be in a 2D arrangement (i.e. a monolayer). Note the previously submitted Declarations, which illustrate the understanding of ordinarily skilled artisans to this effect. Nevertheless, amendments to incorporate this language are made to simplify issues and expedite this case.

identifying substances, more specifically a scanning spectrophotometer for use in detecting fluorescence in liquid samples to identify compounds therein. The field of spectrophotometry (and more generally analytical instrumentation) is an entirely different field from that of the present invention. This is in part demonstrated by the fact that the US search classification (356/318) of US02/0109841 is completely different from that of the other primary art cited in this case (classification 435/6).

Second, and more importantly, a careful reading of US02/0109841 will show that the Examiner reads the reference out of context. Note that the passage relied upon by the Examiner, at the end of paragraph 0046 of US02/0109841, refers to

> collecting the emission light from the sample in a microtiter well or on a two dimensional surface such as a glass microscope slide, polyacrylamide gel, silicon microarray or other solid surfaces.

The reference is discussing the *collection of emission light which is emitted from a surface* of the material being analyzed (or from a surface of a medium containing the material being analyzed). When read in context, it is clear that nucleic acids are *within* the three-dimensional matrix of a thin gel, and light *from the surface* of the gel – where emission occurs – is spectrophotometrically analyzed. In this context, a polyacrylamide gel may be regarded as a "surface"; however, in the context of nucleic acid hybridization, a gel is regarded as a three-dimensional matrix. US2002/0109841 therefore does not support the assertion that oligonucleotides bound within the volume of a gel are bound to a solid *surface*.

2.a.ii. Drobyshev, When Viewed in Context, Does Not Disclose or Suggest that a Polyacrylamide Gel is a Solid Surface

The Examiner also states that *Drobyshev* regards a polyacrylamide gel to be a solid surface, noting *Drobyshev*'s statement at page 48, column 1 that the reaction "looks more like a liquid phase than a solid phase interaction", and that the "[p]olyacrylamide gel provides a stable three dimensional support for immobilized oligonucleotides". However, the same statements in fact illustrate *Drobyshev*'s understanding that the immobilized oligonucleotides are arranged *within* the body of the gel pad *in a three dimensional arrangement*. Oligonucleotides immobilized in this way are not bound to a "surface" as that term is commonly understood to an ordinary artisan.

Additionally, the three dimensional arrangement of oligonucleotides is essential to the working of the *Drobyshev et al* method and is not simply an equivalent to a single layer of oligonucleotides bound to a solid surface. For example, page 48 of *Drobyshev et al* states (at first column, midway down):

> The polyacrylamide gel provides more than 100 times greater capacity for three dimensional immobilization of oligonucleotides than does a two dimension glass surface. The high concentration of immobilized oligonucleotides facilitates the discrimination of mismatch duplexes and enhances the sensitivity of measurements on the microchips.

The polyacrylamide gel is thus used in *Drobyshev et al precisely because it is not a solid surface*, in order to immobilize oligonucleotides in a three dimensional array to increase binding capacity, and thus increase sensitivity. This further demonstrates that an ordinary artisan would not modify *Drobyshev et al* to bind oligonucleotides to a solid surface; see MPEP 2143.01 (subsection entitled "The Proposed Modification Cannot Render The Prior Art Unsatisfactory For Its Intended Purpose").

2.a.iii. As Evidenced by Dictionary Definitions, One of Ordinary Skill in the Field of the Invention Would Not Understand the Ordinary Meaning of "Solid Surface" as Encompassing a Polyacrylamide Gel

The Examiner states that the ordinary meaning of "solid surface" would be understood as encompassing a polyacrylamide gel, noting that "solid" is regarded as meaning neither a liquid nor a gas.[2] The Examiner then dismisses the dictionary definitions of "surface" provided by the Applicant, stating that they "obscure more than they illuminate," and implying that these definitions *admit* that a polyacrylamide gel is a "surface" since these definitions include "layer" (which would encompass a gel). However, kindly review the definitions more closely; this is not in fact the case.

[2] This definition defines a solid by what it is *not*, rather than what it *is*, and thereby does not directly address the issues here. Consider that by the same reasoning, a liquid is neither a solid nor a gas, and thus a gel – not being a "solid" either, and rather being in a phase between solid and liquid – could be regarded as a liquid instead (since it is neither solid nor gas). Nevertheless, if it would be of assistance to attain allowance, the claims could be amended to recite "entirely solid-phase" rather than merely "solid".

As previously noted, where a claim term is an everyday word which is not assigned a special or limited meaning by the specification, the Court of Appeals for the Federal Circuit has stated that a dictionary should be used to determine the meaning that should be given to the term.[3] The Applicant presented dictionary entries defining a "surface" as:

- the outer or top part or layer of something

  (Cambridge International Dictionary of English, http://dictionary.cambridge.org/define.asp?key=surface*1+0)

- the exterior or upper boundary of an object or body

  (Merriam Webster's Collegiate Dictionary, 10th Edition, http://www.m-w.com/cgi-bin/dictionary?book=Dictionary&va=surface)

- 1a. The outer or the topmost boundary of an object. b. A material layer constituting such a boundary.

  (The American Heritage Dictionary of the English Language, http://www.bartleby.com/61/29/S0912900.html)

- the outer part or external aspect of an object

  (Dorland's Illustrated Medical Dictionary, http://www.mercksource.com)

- The exterior part of anything that has length and breadth; one of the limits that bound a solid, especially. The upper face; superficies; the outside.

  (The On-line Medical Dictionary, http://cancerweb.ncl.ac.uk/cgi-bin/omd?surface)

When the definitions are fully read, it is seen that they do not state that a "surface" is simply a "layer" – rather, a "surface" is an *"outer," "top," "exterior," "upper,"* etc. "layer." In other

[3] E.g., *Optical Disc Corp. v. Del Mar Avionics*, 54 USPQ2d 1289, 1295 (Fed. Cir. 2000); *Vanguard Products Corp. v. Parker Hannifin Corp.*, 57 USPQ2d 1087, 1089 (Fed. Cir. 2000).

words, a "surface" is a bounding face. Kindly consider the full definitions in context, and it is seen that oligonucleotides arrayed within a gel (as in *Drobyshev*) do not constitute oligonucleotides bound to a surface.

2.a.iv. As Evidenced by the Kwok and Mirzbekov Declarations, One of Ordinary Skill in the Field of the Invention Would Not Understand the Ordinary Meaning of "Solid Surface" as Encompassing a Polyacrylamide Gel

As further evidence that ordinary artisans do not regard gels with immobilized oligonucleotides as being "solid surfaces" with bound oligonucleotides, the Applicant provided Declarations of Professor Pui-Yan Kwok of the University of California-San Francisco and Professor Andrei Mirzabekov of the Engelhardt Institute in Moscow (whose group produced the *Drobyshev* paper in issue in this case). These Declarations do not appear to be addressed.[4] The Kwok Declaration notes at Section 4, Page 2 that

> Oligonucleotides within a gel are disposed in a three-dimensional and random arrangement and an ordinarily skilled artisan would not consider that these gel-immobilized oligonucleotides are 'bound to a solid surface'.[5]

Professor Kwok therefore does not regard a gel with immobilized oligonucleotides to be a solid surface with bound oligonucleotides. Further, the Mirzabekov Declaration – from a co-author of *Drobyshev* – states in its first paragraph:

> ...there are fundamental differences between the hybridization kinetics, chemistry and capacity of solid surface 2D reaction surfaces compared to 3D supports comprised of gel matrices. Specifically, whereas a 2D surface is planar without significant liquid volume, a 3D support comprises ~95% liquid volume.

It is clear that Professor Mirzabekov does not consider oligonucleotides bound within a gel matrix support to be "bound to a solid surface", and that he regards solid surfaces and gels to be

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[4] This is unclear; it is stated at page 9 of the April 8, 2003 Office Action that "[t]he declaration is addressed by the understanding of the ordinary artisan as discussed above." With respect, this statement is not understood (i.e., which Declaration, if any, is being referred to, and how it is regarded as being "addressed").

[5] Since the Applicant has now submitted ***two*** expert Declarations testifying to the unobviousness of the claimed invention – one of these, from Mirzabekov, being from the same group that produced *Drobyshev et al.* – kindly grant their contents close attention (particularly since these are difficult and expensive to obtain).

physically very different. As a co-author of the cited *Drobyshev* reference, his Declaration should be given due weight. His Declaration proceeds to summarize other publications which illustrate that gel immobilized array hybridization is indeed regarded as a liquid phase system. For example, *Livshits et al.*, J. Biomol. Structure Dynam. (1994) 11 783-795 states:

> This dependence [of duplex thermostability on concentration] is specific for oligonucleotides immobilized in the gel volume (3-D immobilization) rather than on a flat surface of a filter or glass (2-D immobilization).

Note that this explicitly distinguishes a "gel volume" from a "flat surface."[6] Also note Professor Mirzabekov's citation of *Kochinsky and Mirzabekov*, Human Mutation (2002) 19:343-360 (p. 344), which states that "each pad behaves as an individual nanoliter or smaller test tube", further illustrating that gel pads are regarded as three-dimensional, effectively liquid phase media.

The Declaration evidence directly rebuts the assertion that the gel immobilized microarray hybridizations of *Drobyshev* are "solid phase" hybridizations, and illustrate that the understanding in the art – as illustrated by a co-author of *Drobyshev* – is clearly that gel immobilized microarray hybridizations are distinct from solid phase hybridizations.

2.a.v. One of Ordinary Skill in the Field of the Invention Would Not Understand the Ordinary Meaning of "Bound" as Encompassing an Oligonucleotide "Indirectly" Bound to Glass By a Polyacrylamide Gel

The Examiner presented a new issue at pages 9-10 of the Office Action, contending that the broadest reasonable interpretation of "bound" encompasses both "direct binding" and "indirect binding" (with the latter encompassing a *Drobyshev* arrangement wherein oligonucleotides are "indirectly" bound to glass by a polyacrylamide gel). Kindly reconsider for reasons similar to those noted above. With all respect, the Examiner's interpretation is not reasonable: one of ordinary skill would not regard oligonucleotides immobilized within a gel on a glass surface as being "bound to a solid surface" (the glass), in the same sense that one would not regard chaining a bicycle to a post in the ground as providing a bike "bound to the ground" as opposed to a bike

[6] In similar respect, the same paper later states "[o]ur approach to sequencing by hybridization based on oligonucleotide immobilization within a gel volume has several advantages in comparison with the immobilization on a flat surface, for example a glass or membrane one."

"bound to the post." Stated more simply, the term "bound to a solid surface" would not be regarded as encompassing the Examiner's "indirect" binding unless the word "indirectly" (or some similar term) is inserted as a qualifier. This can be seen with reference to the definition of "bound" (or its present participle "bind") in the aforementioned online dictionaries, and particularly with reference to the foregoing passages of the Kwok and Mirzabekov Declarations, which clearly illustrate that ordinary artisans do not regard *Drobyshev*'s oligonucleotides as being bound to a solid surface. It is also notable that it appears (from a review of all prior communications regarding this application) that the Examiner did not heretofore contemplate "bound to a solid surface" as encompassing indirect binding via a gel. This delay in construing "bound" as encompassing indirect binding is further evidence that one of ordinary skill would not understand "bound" as emcompassing such binding.

Therefore, in view of the ordinary understanding of those in the art,[7] and further in view of the prior interpretation given to "bound to a solid surface" by the Applicant and Examiner,[8] oligonucleotides within a gel, with the gel being provided on glass (as in *Drobyshev*), do not constitute oligonucleotides "bound to a solid surface."

2.a.vi. In Summary

In summary, the foregoing comments illustrate that when the cited references are read in context, when the dictionary definitions are read in full, and when the views of those of ordinary skill in the art of nucleic acid hybridization are considered, "a single DNA strand bound to a solid surface" does not encompass the *Drobyshev* arrangement of an oligonucleotide immobilized within the interior of a polyacrylamide gel, with the gel being situated on glass. Therefore, even if a suggestion to combine *Drobyshev* and *Wittwer* existed, the claimed invention would not result from

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[7] "Although the PTO must give claims their broadest reasonable interpretation, this interpretation must be consistent with the one that those skilled in the art would reach." *In re Cortright*, 49 USPQ2d 1464, 1467 (Fed. Cir. 1999).

[8] See, e.g., *Inverness Med. Switz. Gmbh v. Princeton Biomeditech Corp.*, 64 USPQ2d 1926, 1931-32 (Fed. Cir. 2002) ("[t]he prosecution history limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution.") In this respect, *to the extent any uncertainty exists, **it is hereby explicitly stated that the claim terminology "bound to a solid surface" is not to be regarded as encompassing oligonucleotides within a gel situated on a solid surface.***

the combination.

2.b. *Drobyshev*, Even if Modified to Use SYBR Green for Detection, Does Not Amount to the Claimed Method

At page 10, the Examiner states:

> The modification necessary to render the claims obvious is not three dimensional versus two dimensional nature of the array. The modification to *Drobyshev* is the use of SYBR green dye for detection. The rejection provides strong motivation to detect using SYBR Green.

However, for the reasons noted above, the claims are plainly addressed to 2D hybridization – a feature important to the Applicant's goal of dynamic, real-time measurement of hybridization with good signal measurement – whereas *Drobyshev* is addressed to 3D hybridization. In the presently claimed methods, the target sequence is immobilized in a 2D array and the probe is free in solution. In *Drobyshev*, the probe sequences (10 mer oligonucleotides) are immobilized in a 3D array within a polyacrylamide gel and the target sequence is free to diffuse into the gel. Even if the *Drobyshev* method incorporated the use of SYBR Green, the modified method would not be encompassed by the present claims (since it is not executed on a surface), and thus the claimed methods are not obvious.

2.c. One of Ordinary Skill Would Also Not be Motivated by *Wittwer* to use SYBR Green in *Drobyshev*'s Method

As noted in the foregoing Section 2.b of this Response, *Drobyshev* would not amount to the claimed method even if modified to use SYBR Green. However, even if it *did* amount to the claimed method if so modified, *Wittwer* does not in fact offer objective evidence motivating one of ordinary skill to make such a modification. The Examiner states that such a motivation exists because:

> *Drobyshev* expressly monitors hybridization by measurement of melting curves, just as *Wittwer* does, and the advantages disclosed by *Wittwer* in the use of SYBR green would be directly applicable and expected to apply to the *Drobyshev* method.

However, there are significant differences between the methods of *Wittwer* which employ SYBR Green and the methods of *Drobyshev*. In fact, neither *Wittwer* nor *Drobyshev* teach the use of *any* intercalating dye to detect DNA sequence variation; rather, SYBR Green is used in a different

process for different purposes. *Wittwer* employs SYBR Green for fluorescent monitoring of the production of dsDNA in PCR reactions (c110bp products):

> Melting peaks can distinguish specific products from non-specific products .... and they can distinguish two .... purified PCR products mixed together so they should also be useful for distinguishing two specific products amplified together in a single reaction tube.

(See col. 40 line 53 onward.) This is distinct from allelic discrimination by measuring the melting curves of gel immobilized oligonucleotide duplexes (10mers), which is described in *Drobyshev*. DNA molecules in the *Wittwer* PCRs are much longer, are free in solution, and are highly concentrated relative to the oligonucleotides of *Drobyshev*. There is no guidance in either disclosure about whether SYBR green provides sufficient sensitivity for allelic discrimination using mismatch oligonucleotides and this sensitivity could not be predicted from the production of melting curves for PCR products. *Wittwer* then goes on to state that:

> When sequence specific detection and quantitation are desired, resonance energy transfer probes can be used instead of double strand specific DNA dyes. The Tm of hybridization probes shifts 4-8° C if a single base mismatch is present. If a hybridization probe is placed at a mutation site, single base mutations are detectable as a shift in the probe melting temperature.

(Col. 40 lines 53-59.) In other words, if a skilled person wants to perform sequence specific detection and/or quantitation, *Wittwer* teaches the use of labeled hybridization probes and FRET assays. There is plainly no *clear* and *objective* suggestion that SYBR Green should be used in detection,[9] and at the time of the invention, a skilled artisan could not expect SYBR Green could to apply to the Drobyshev method without considerable additional experimentation.

While the Examiner accuses us of relying overmuch on *Wittwer*'s FRET assay embodiment, with respect, this is the relevant embodiment of *Wittwer*: it relates to detection, whereas *Wittwer*'s SYBR Green assay does not. There is *no* embodiment described in *Wittwer*, either preferred or

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[9] *Winner International Royalty Corp. v. Wang*, 53 USPQ2d 1580, 1586 (Fed. Cir. 2000) (citations and footnotes omitted):

> When an obviousness determination is based on multiple prior art references, there must be a showing of some "teaching, suggestion, or reason" to combine the references. .... Although a reference need not expressly teach that the disclosure contained therein should be combined with another, the **[1587]** showing of combinability, in whatever form, must nevertheless be 'clear and particular.'"

non-preferred, which employs SYBR Green to perform sequence variation detection and/or quantitation. There is certainly nothing in *Wittwer* itself which would teach a skilled person to use SYBR Green for discriminating the melting curves of short immobilized oligonucleotides in the detection of DNA variation; any artisan who followed this approach would be ignoring the teaching of *Wittwer* as described above and exemplified in Examples 18-23. And *Drobyshev et al* does not mention or suggest the possibility of replacing the fluorescent label with any intercalating agent for the determination of the Tm of the probe/target complex. Without any objectively ascertainable suggestion to utilize *Wittwer*'s SYBR Green in *Drobyshev*'s method, the rejection is formulated in hindsight, and the rejections should be withdrawn for this reason and those noted in the foregoing Sections 2.a and 2.b of this Response.

3. Section 3 of the Office Action: Rejection of Claims 1-5, 7, 8, 10-18, 20, 21, 23-31, 33, 34, 36-44, 46, 47, 49-52 and 67-70 under 35 USC §103(a) in view of *Drobyshev et al* (Gene (1997) 188:45-52, U.S. Patent 6,174,670 to *Wittwer*, and U.S. Patent 6,048,690 to *Heller et al*

These rejections are understood to build upon the foregoing rejections by further rejecting 7, 20, 33, and 46 in view of *Heller*. The Examiner indicates that *Heller* is relied upon solely to teach that biotin-streptavidin binding to surfaces is known, and therefore that the use of a biotin-streptavidin linkage in a hybridization method of *Drobyshev* which employed the intercalating dye of *Wittwer* would be obvious. All claims are submitted to be allowable for the reasons noted in the foregoing Section 2 of this Response, but even assuming the independent claims were obvious in view of *Drobyshev* and *Wittwer*, it is submitted that *Heller* does not supply a motivation which would render obvious claims 7, 20, 33 and 46.

The Examiner points to page 45 column 2 of *Drobyshev* as providing motivation for use of biotin/streptavidin. However, not only is this section discussing oligonucleotide arrays generally (and not specifically gel pads), but it refers merely to manufacture by "parallel synthesis of oligonucleotides or by chemical immobilization". There is nothing here which would motivate a skilled person to use a biotin/strepavidin linkage, still less to use such a linkage in the context of a polyacrylamide gel. In *Drobyshev*, probe oligonucleotides are chemically bound to the

polyacrylamide matrix. When the references are objectively viewed, an ordinary artisan would see no reason to attempt to immobilize the probe oligonucleotides in any other way. Further, even if an artisan wished to employ a *Heller* biotin/streptavidin linkage in a *Drobyshev* 3D gel immobilized microarray (for whatever reason), it is unclear how a skilled artisan could do so. A biotin/streptavidin linkage is simply incompatible with the immobilization of microarrays in polyacrylamide gels.

4. Section 4 of the Office Action: Rejection of Claims 1-6, 8-19, 21-32, 34-45, 47-52, and 67-70 under 35 USC §103(a) in view of *Drobyshev et al* (Gene (1997) 188:45-52), U.S. Patent 6,174,670 to *Wittwer*, and U.S. Patent 5,789,167 to *Konrad et al.*

Regarding claims 9, 22, 35, and 48, the Examiner contends that it would have been obvious to one of ordinary skill to utilize the Hepes buffer of *Konrad* in the detection method of *Drobyshev* (as modified by *Wittwer*), since *Konrad* allegedly expressly teaches that Hepes is an equivalent buffer. All claims are submitted to be allowable for the reasons noted in Section 2 of this Response, but it is submitted that claims 9, 22, 35, and 48 are allowable even if their parent claims are not.

The claims in issue are drawn to buffers with salt concentrations less than 200mM, in particular Hepes buffers of this type. Such buffers have been found to offer advantageous properties in the present methods, as described on page 10 lines 20-31 of the specification. In *Konrad* (which uses a Tris buffer) and the art in general, high salt buffers are used for nucleic acid hybridization, and there is no suggestion whatsoever of any advantages that might be attained by a lower concentration. Without an indication of any suggested advantages in the prior art of the use of a low salt buffer of the type claimed, the rejection should be withdrawn.

5. New Claims

New claims 71-76 are submitted to be allowable for at least the reasons noted above; note that they recite more specific limitations in several respects, which further assist in differentiating the claims from the cited references.

6. In Closing

If any questions regarding the application arise, please contact the undersigned attorney. Telephone calls related to this application are welcomed and encouraged. The Commissioner is authorized to charge any fees or credit any overpayments relating to this application to deposit account number 18-2055.

For the Applicant,

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ATTACHMENTS:

- PTO-2038 ($343)